SUPPORT FOR THE AMENDMENT

Claims 1-30, 32-34 and 36-40 were previously canceled.

Claims 31, 56, and 57 have been amended.

The amendment of Claim 31 is supported by the corresponding claims as previously filed, as well pages 10-49 as originally filed, including page 14, line 7 to page 15, line 2 and page 41, lines 8-17. The amendment of Claims 56 and 57 is supported by the corresponding claims as previously filed, as well the original specification, for example, at page 22, line 22 to page 23, line 27.

No new matter has been entered by the present amendment.

REMARKS

Claims 31, 35, and 41-59 are pending in the present application.

At the outset, Applicants wish to thank Examiner Fronda for the helpful and courteous discussion with their undersigned Representative on February 24, 2009. During this discussion, the Examiner agreed that the IDS filed on May 5, 2008 would be considered since it was properly filed (the Examiner acknowledged consideration of this IDS on March 2, 2009). Also during this discussion, the amendments to Claims 31, 56, and 57 presented herein were discussed, as well as the possibility of presenting experimental data. The content of this discussion is reflected in the amendments and remarks herein.

Applicants also wish to thank Examiner Fronda for the indication that Claims 44, 47, 49, 50, and 52-55 are allowable.

Reconsideration of the outstanding rejections is requested.

The rejection of Claims 56 and 57 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

Applicants have amended Claims 56 and 57 to specify that "replacement of the amino acid residue Arg-378 and subsequent amino acid residues with the amino acid sequence of SEQ ID NO: 29" means "replacement of the amino acid residues 378-384 with the amino acid sequence of SEQ ID NO: 29" thus making clear what was intended by "and subsequent". Withdrawal of this ground of rejection is requested.

The rejection of Claims 31, 35, 41-43, 45, 46, 48, 51, 58, and 59 under 35 U.S.C. §103(a) over Michaeli et al in view of Parsot et al, Malumbres et al, Greene, and Park et al is respectfully traversed.

Claims 31, 35, 41-43, 45, 46, 48, 51, 58, and 59 are rejected as being unpatentable over Michaeli et al, in view of the combined teachings of Parsot et al, Malumbres et al, Greene, and Park et al.

In the Office Action, the Examiner continues to recognize that Michaeli et al differs from the claimed invention, at least, in that this reference does not teach a recombinant *Escherichia* bacterium deficient in the metJ gene encoding a repressor of the L-methionine biosynthesis gene. The Examiner alleges that Greene teach the E. coli repressor of the L-methionine biosynthesis system encoded by the metJ gene. The Examiner further alleges that Park et al teach the enzyme *E. coli* metK gene encoding S-adenosylmethionine synthetase which catalyzes the synthesis of S-adenosyl-L-methionine (SAM), where SAM is a major methyl group transfer agent in biological systems and the methyl moiety of SAM is transferred to proteins, lipids, nucleic acids, and vitamins by SAM-dependent methyltransferases.

However, in Park et al, the central theme is the enzymatic synthesis of SAM using S-adenosylmethionine synthetase encoded by the metK gene. This enzyme is subject to product inhibition. To avoid the problem, Park et al searched additives which overcome product inhibition of the enzyme as summarized in Table 1. Thus, an object and standpoint of Park et al are completely different from those of the present invention or other cited references.

What is missing in Park et al, and the other cited references, is that it does not disclose or suggest disruption of the metK gene and application of this gene to breeding of L-methionine producing strains. At best, the Examiner's case can be summarized as that the in view of the

relied upon references the artisan would have the capabilities to practice the claimed invention. However, it is well settled that whether the claimed invention is within the capabilities of one of ordinary skill in the art is not sufficient by itself to establish *prima facie* obviousness (MPEP §2143.01). Indeed, the mere fact that the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993).

In the present case, looking at the disclosure of Park et al to determine whether this reference actually provides a disclosure of disruption of the metK gene and application of this gene to breeding of L-methionine producing strains, the artisan sees that Park et al disclose that S-adenosylmethionine synthetase is subject to product inhibition. Since increased product formation would shut down the enzymatic activity, the skilled artisan would not be motivated to disrupt the metK gene absent a specific disclosure that L-methionine producing strains do not suffer from the above-mentioned product inhibition, or the inhibition is desensitized in L-methionine producing strains. Such a disclosure does not exist in the cited art. Accordingly, Applicants submit that even if the artisan were to have Park et al in hand, the combined disclosures of this reference with Michaeli et al and Greene would not be sufficient to render the claimed invention even *prima facie* obvious.

Newly cited references (Parsot et al and Malumbres et al) fail to compensate for the basic deficiencies in the previously cited references (Michaeli et al, Park et al, and Greene). Indeed, Parsot et al and Malumbres et al only disclose that a Thr auxotroph was known, but there is no disclosure in this or any other reference of the specifically claimed invention. At best, the Examiner's case amounts to an allegation that the skilled artisan would have the

general abilities to perform the claimed invention. However, this is the wrong standard for obviousness (MPEP §2143.01).

Moreover, Applicants submit that absent the present application, the artisan would not have been led to the L-methionine production ability of the claimed method. Specifically, reference is made to Example 3, where a metK mutation and metA amplification are performed on various L-threonine auxotrophic strains (WΔBC; see Example 1) and metJ deficient strains (WΔJ and WΔBCΔJ; see Example 1). What is clear from the Table on page 39 of the specification is that introduction of metA amplification into the strains that are either various L-threonine auxotrophic strains or metJ deficient strains provide enhanced production of methionine as compared to amplification of metA in *E. coli* W3110, a derivative of the wild-type K-12 strain of E. coli (see page 26, line 4-6). The production of methionine is further enhanced by the additional mutation of metK to reduce the activity of intracellular S-adenosylmethionine synthetase encoded thereby (see the last two rows of the table on page 39). Applicants further submit that it should be noted that the strain W3110/pMWPthrmetA-W in which the metA gene is amplified did not produce L-methionine (see Table 2). This result indicates that enhancing the metA gene on its own provides no effect. Thus, absent the present specification, this enhanced production of methionine would not have been apparent.

For the reasons above, Applicants submit that even if the artisan were to have Park et al in hand, the combined disclosures of this reference with Parsot et al, Malumbres et al, Michaeli et al, and Greene would not be sufficient to render the claimed invention even *prima facie* obvious.

For the foregoing reasons, withdrawal of this ground of rejection is requested.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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